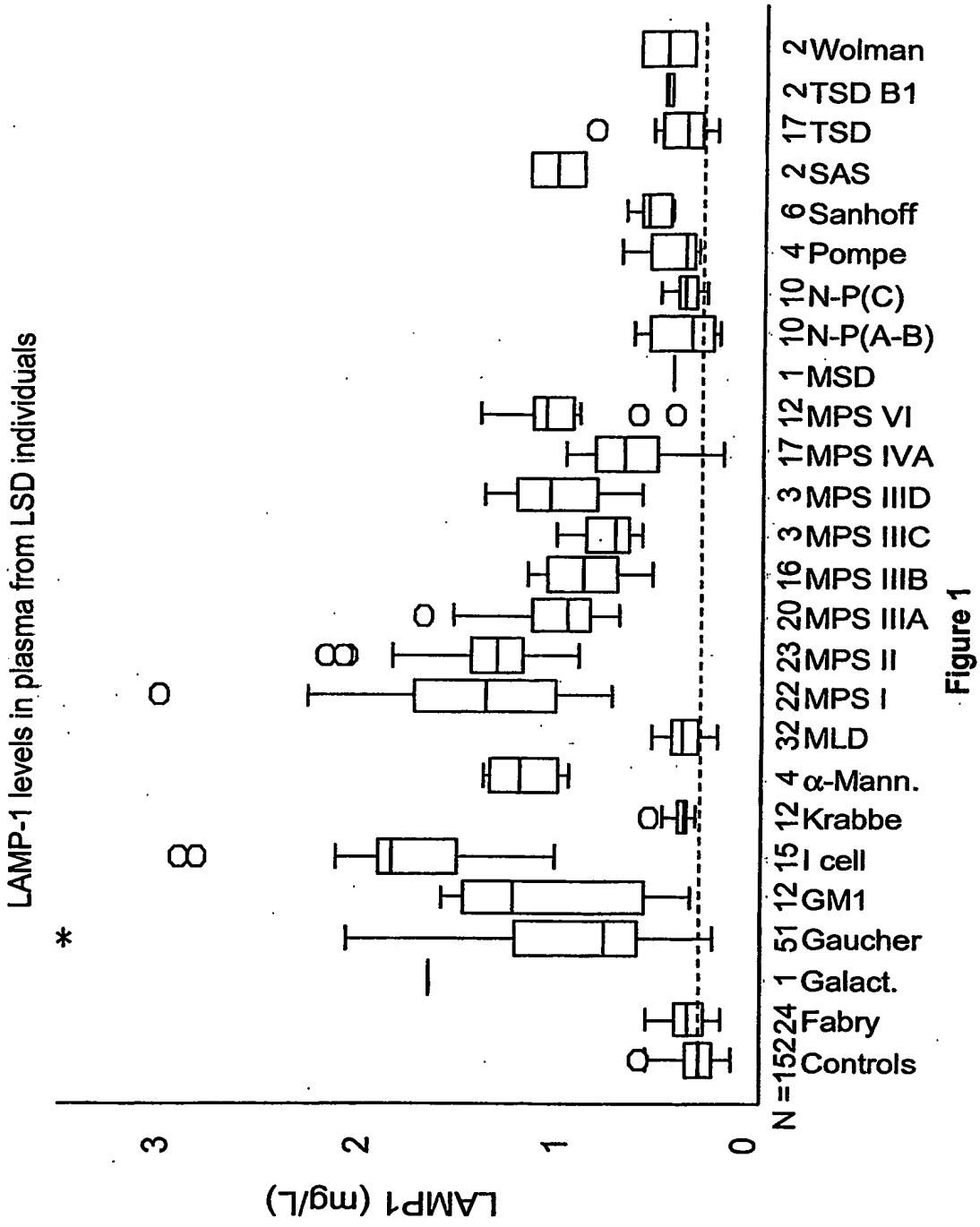
LAMP-1 levels in plasma from LSD individuals
LAMP1 (mg/L)
0
1
2
3
N =
152
24
1
51
12
15
4
12
32
22
23
20
16
3
3
17
12
1
10
10
4
6
2
17
2
2
Controls
Fabry
Galact.
Gaucher
GM1
I cell
Krabbe
α-Mann.
MLD
MPS I
MPS II
MPS IIIA
MPS IIIB
MPS IIIC
MPS IIID
MPS IVA
MPS VI
MSD
N-P(A-B)
N-P(C)
Pompe
Sanhoff
SAS
TSD
TSD B1
Wolman

Figure 1

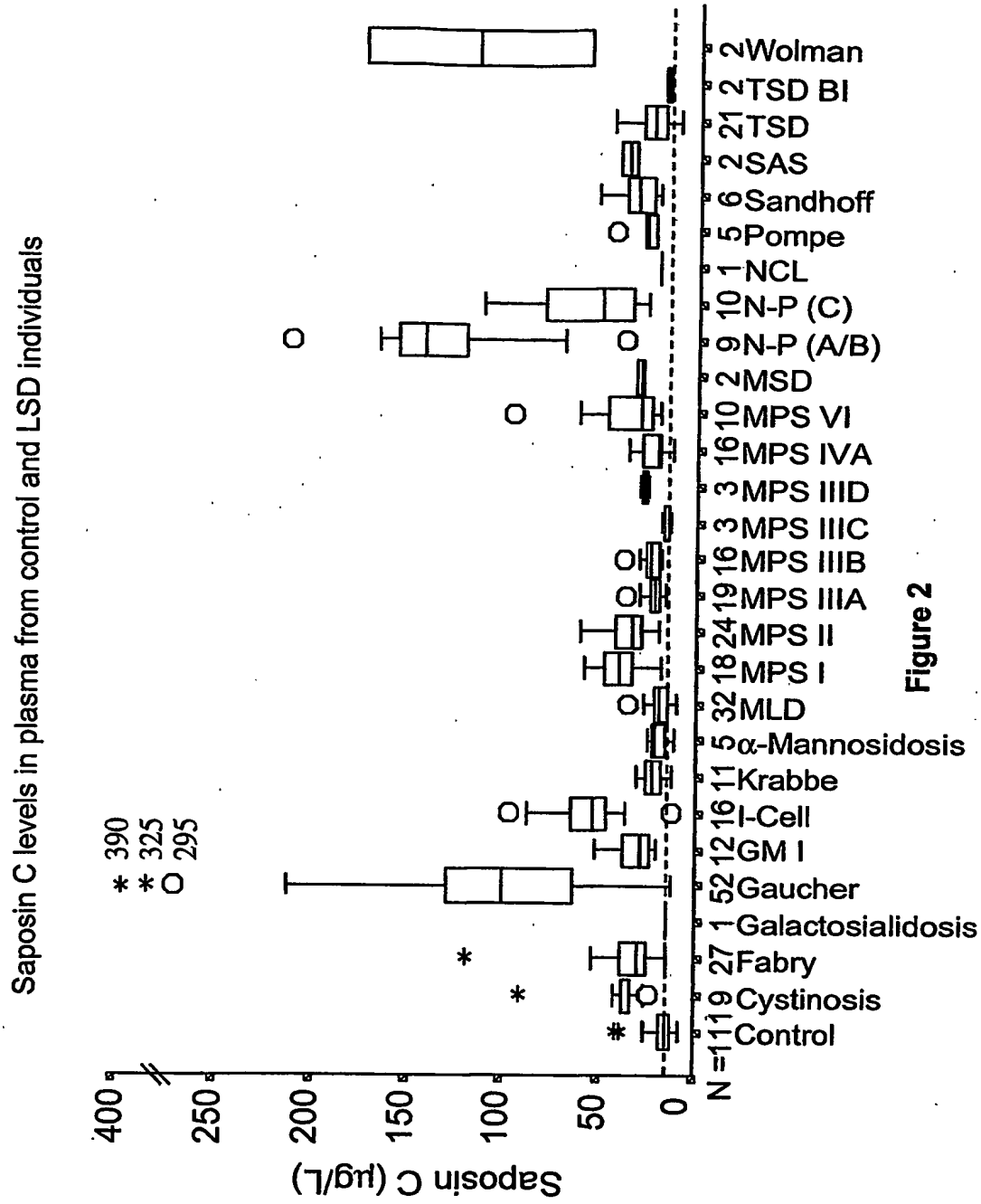
Saposin C levels in plasma from control and LSD individuals
* 390
* * 325
O 295
Saposin C (µg/L)
400
250
200
150
100
50
0
N =
2 Wolman
2 TSD BI
21 TSD
2 SAS
6 Sandhoff
5 Pompe
1 NCL
10 N-P (C)
9 N-P (A/B)
2 MSD
10 MPS VI
16 MPS IVA
3 MPS IIID
3 MPS IIIC
16 MPS IIIB
19 MPS IIIA
24 MPS II
18 MPS I
32 MLD
5 α-Mannosidosis
11 Krabbe
16 I-Cell
12 GM I
52 Gaucher
1 Galactosialidosis
27 Fabry
9 Cystinosis
11 Control

Figure 2

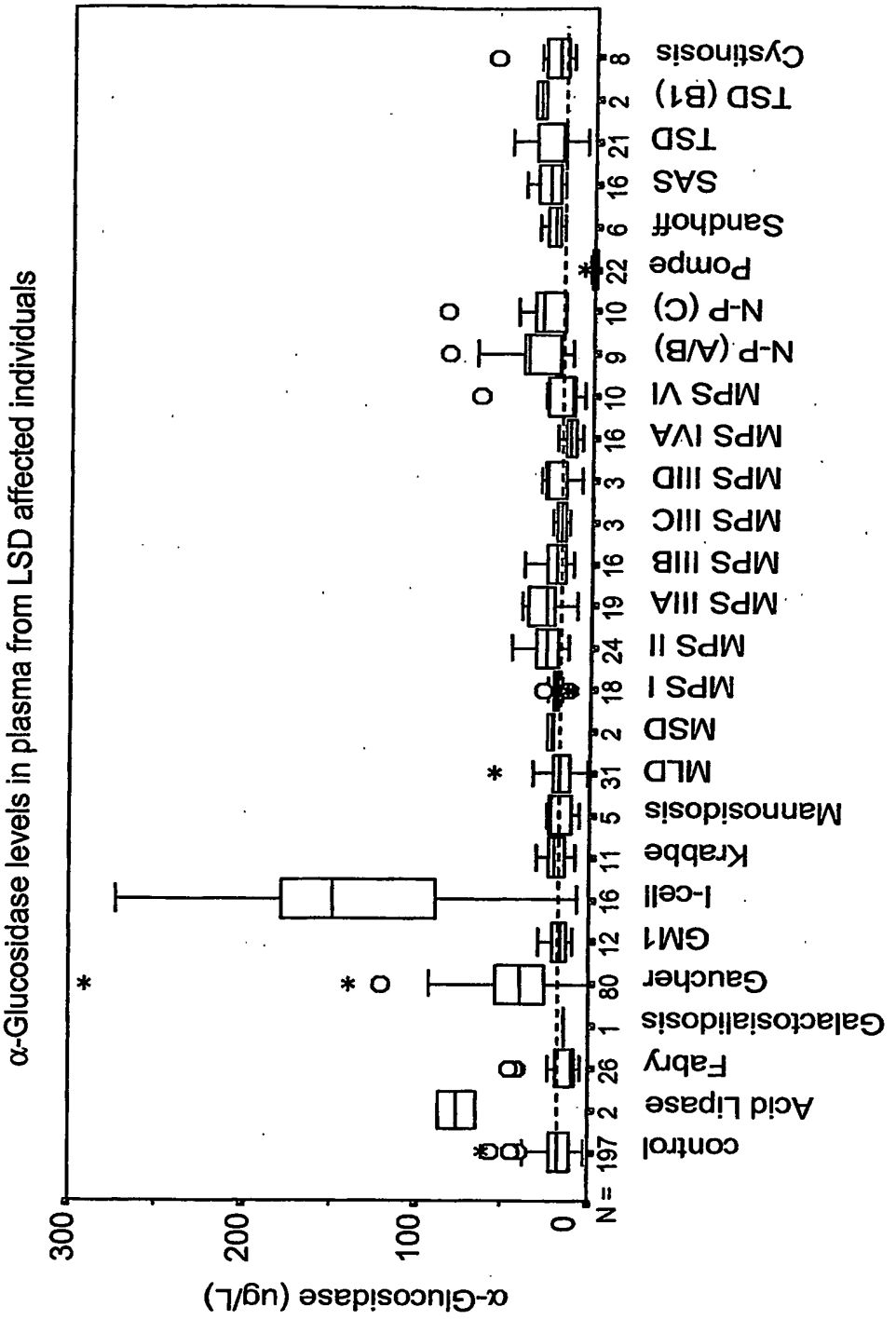
α-Glucosidase levels in plasma from LSD affected individuals
α-Glucosidase (ug/L)
300
200
100
0
N =
197
2
26
1
80
12
16
11
5
31
2
18
24
19
16
3
3
16
10
9
10
22
6
16
21
2
8
control
Acid Lipase
Fabry
Galactosialidosis
Gaucher
GM1
I-cell
Krabbe
Mannosidosis
MLD
MSD
MPS I
MPS II
MPS IIIA
MPS IIIB
MPS IIIC
MPS IIID
MPS IVA
MPS VI
N-P (A/B)
N-P (C)
Pompe
Sandhoff
SAS
TSD
TSD (B1)
Cystinosis

Figure 3

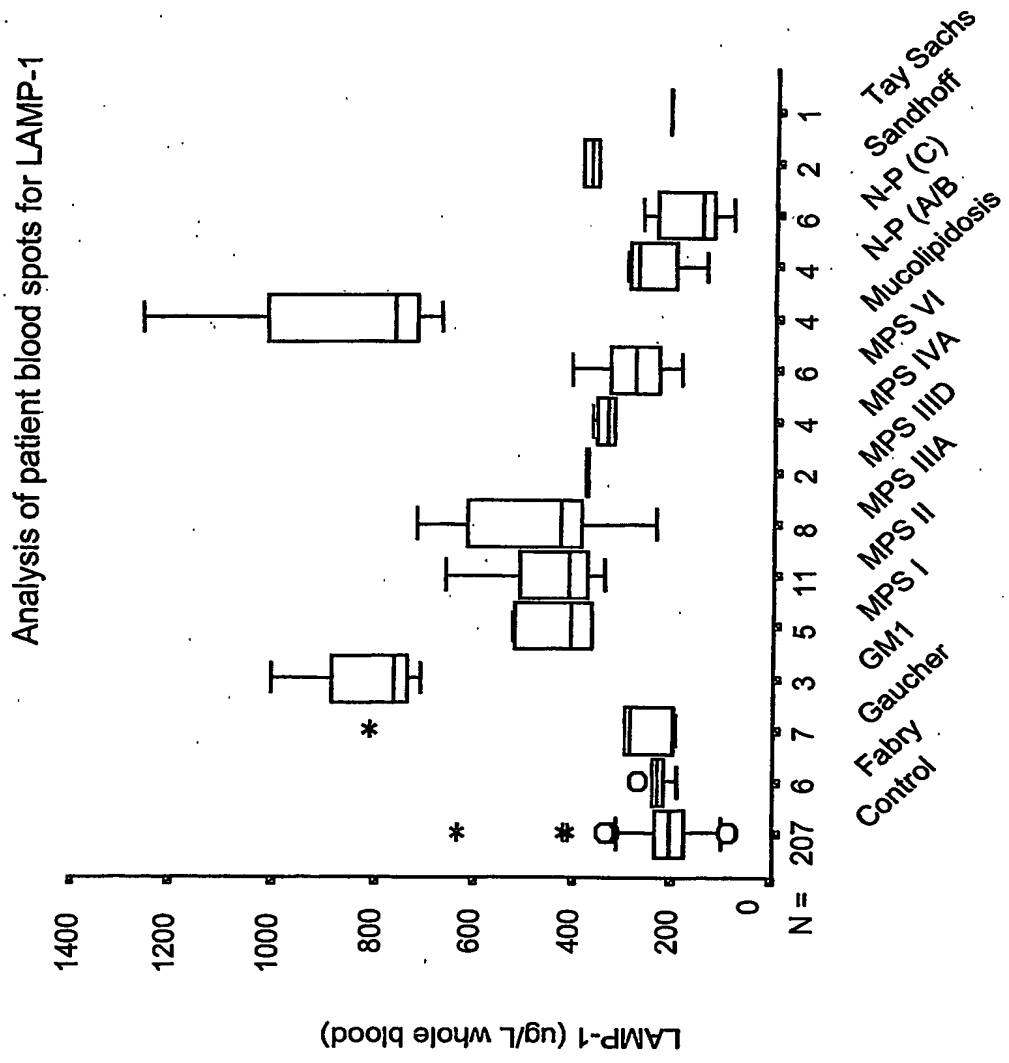
Analysis of patient blood spots for LAMP-1
LAMP-1 (ug/L whole blood)
1400
1200
1000
800
600
400
200
0
N = 207 6 7 3 5 11 8 2 4 6 4 4 6 2 1
Control
Fabry
Gaucher
GM1
MPS I
MPS II
MPS IIIA
MPS IIID
MPS IVA
MPS VI
Mucolipidosis
N-P (A/B
N-P (C)
Sandhoff
Tay Sachs

Figure 4

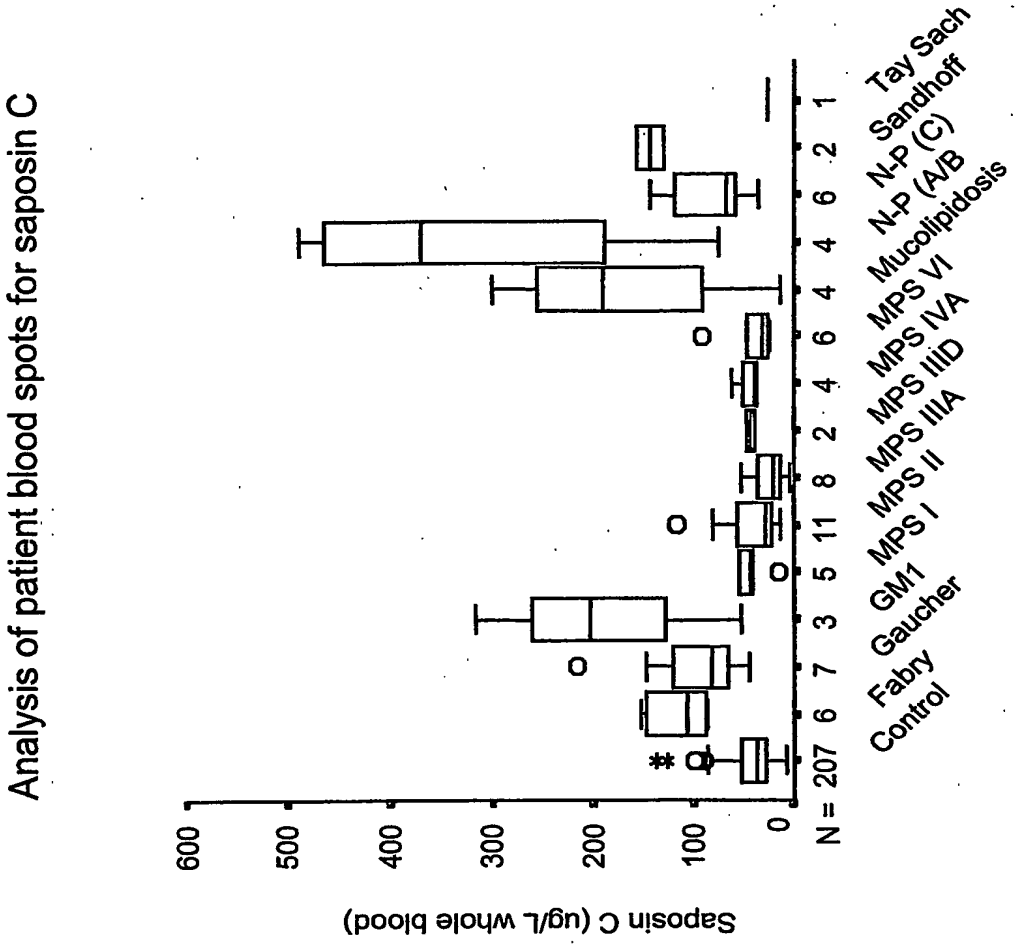
Analysis of patient blood spots for saposin C
Saposin C (ug/L whole blood)
600
500
400
300
200
100
0
N = 207 6 7 3 5 11 8 2 4 6 4 4 6 2 1
Tay Sach
Sandhoff
N-P (C)
N-P (A/B
Mucolipidosis
MPS VI
MPS IVA
MPS IIID
MPS IIIA
MPS II
MPS I
GM1
Gaucher
Fabry
Control

Figure 5

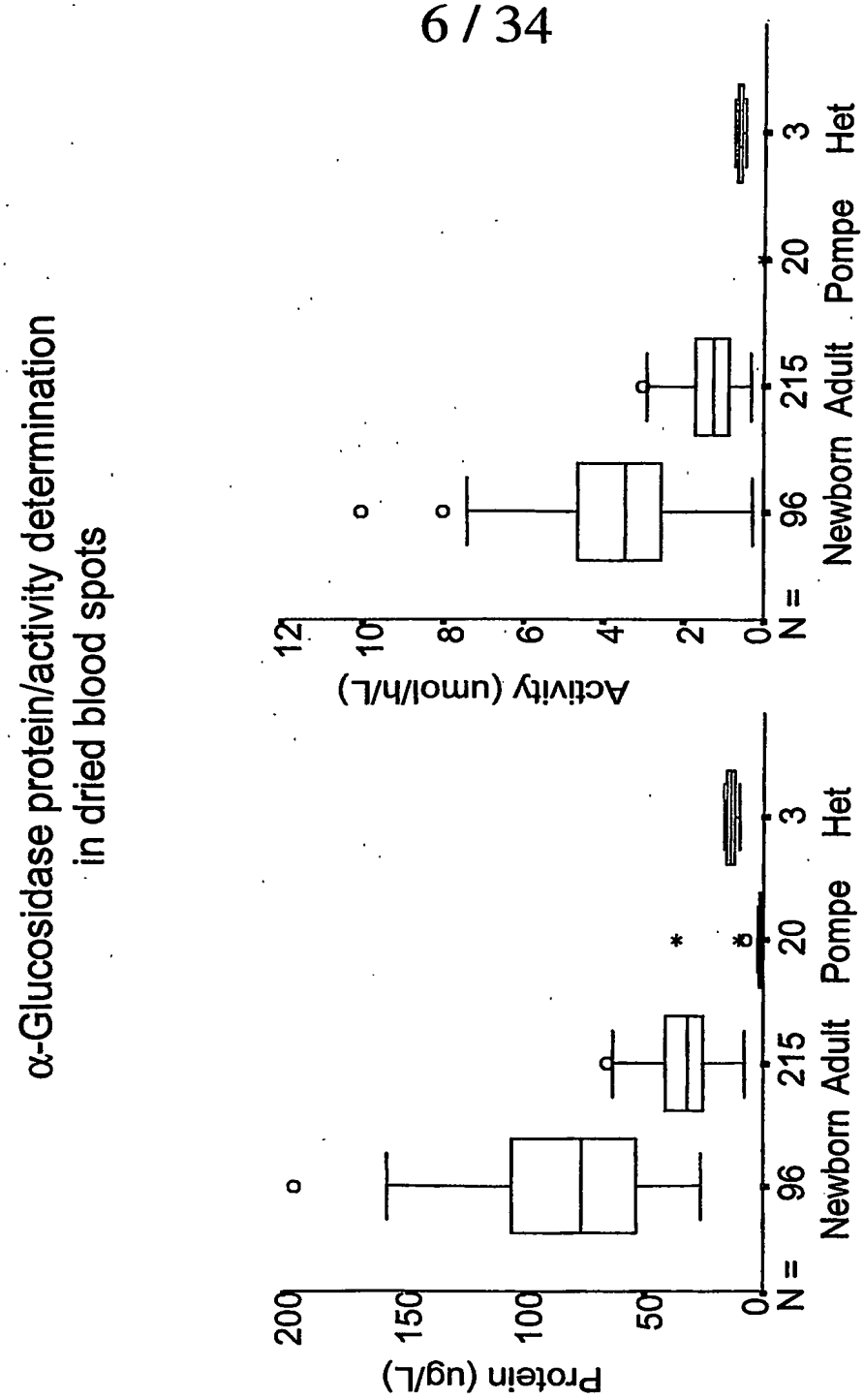
α-Glucosidase protein/activity determination
in dried blood spots
Protein (ug/L)
200
150
100
50
0
Activity (umol/h/L)
12
10
8
6
4
2
0
N = 96 215 20 3
Newborn Adult Pompe Het

Figure 6

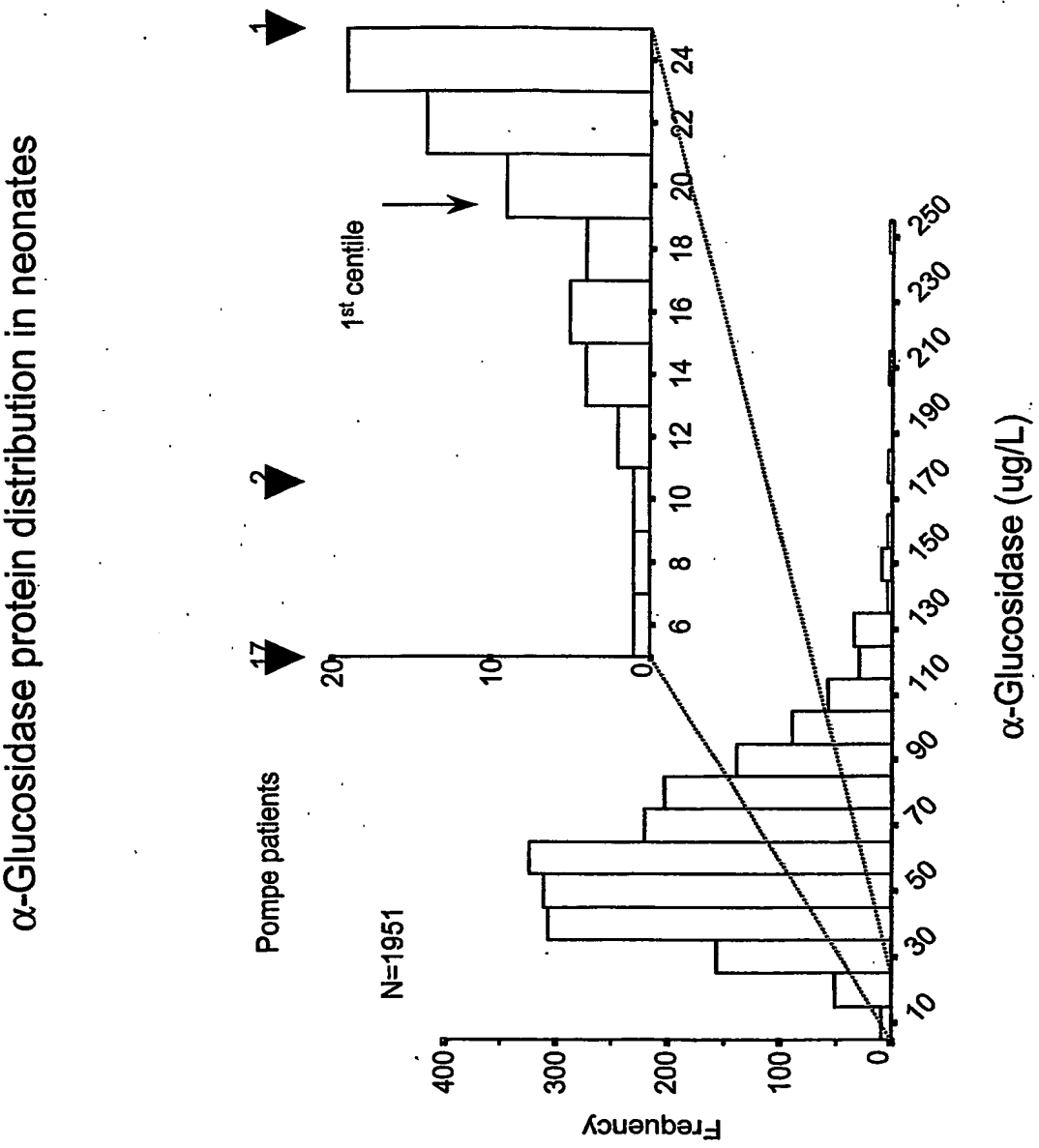
α-Glucosidase protein distribution in neonates
Pompe patients
N=1951
1st centile
Frequency
α-Glucosidase (ug/L)
1
2
17

Figure 7

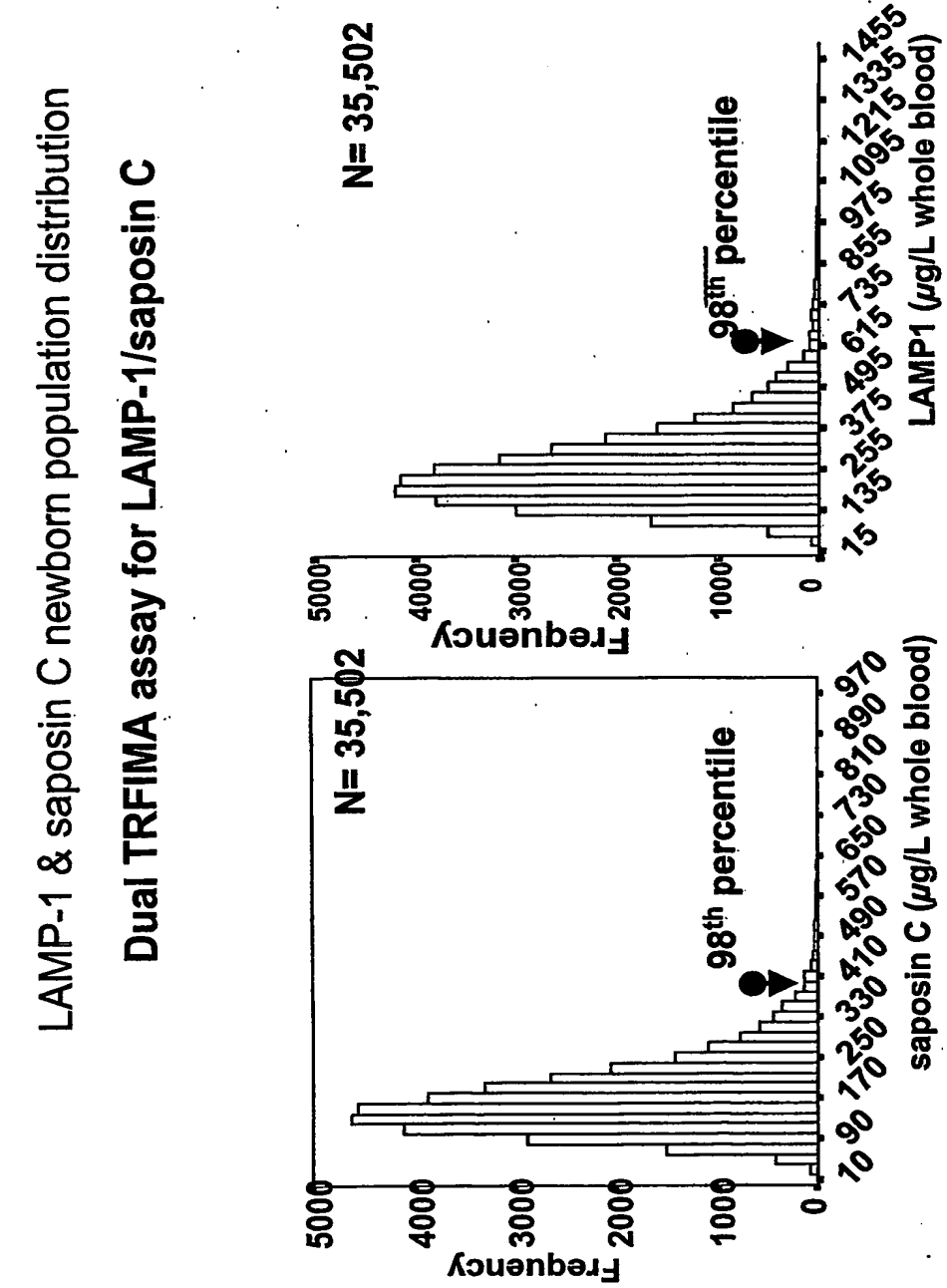
LAMP-1 & saposin C newborn population distribution
Dual TRFIMA assay for LAMP-1/saposin C
N= 35,502
98th percentile
Frequency
5000
4000
3000
2000
1000
0
10 90 170 250 330 410 490 570 650 730 810 890 970
saposin C (µg/L whole blood)
N= 35,502
98th percentile
Frequency
5000
4000
3000
2000
1000
0
15 135 255 375 495 615 735 855 975 1095 1215 1335 1455
LAMP1 (µg/L whole blood)

Figure 8

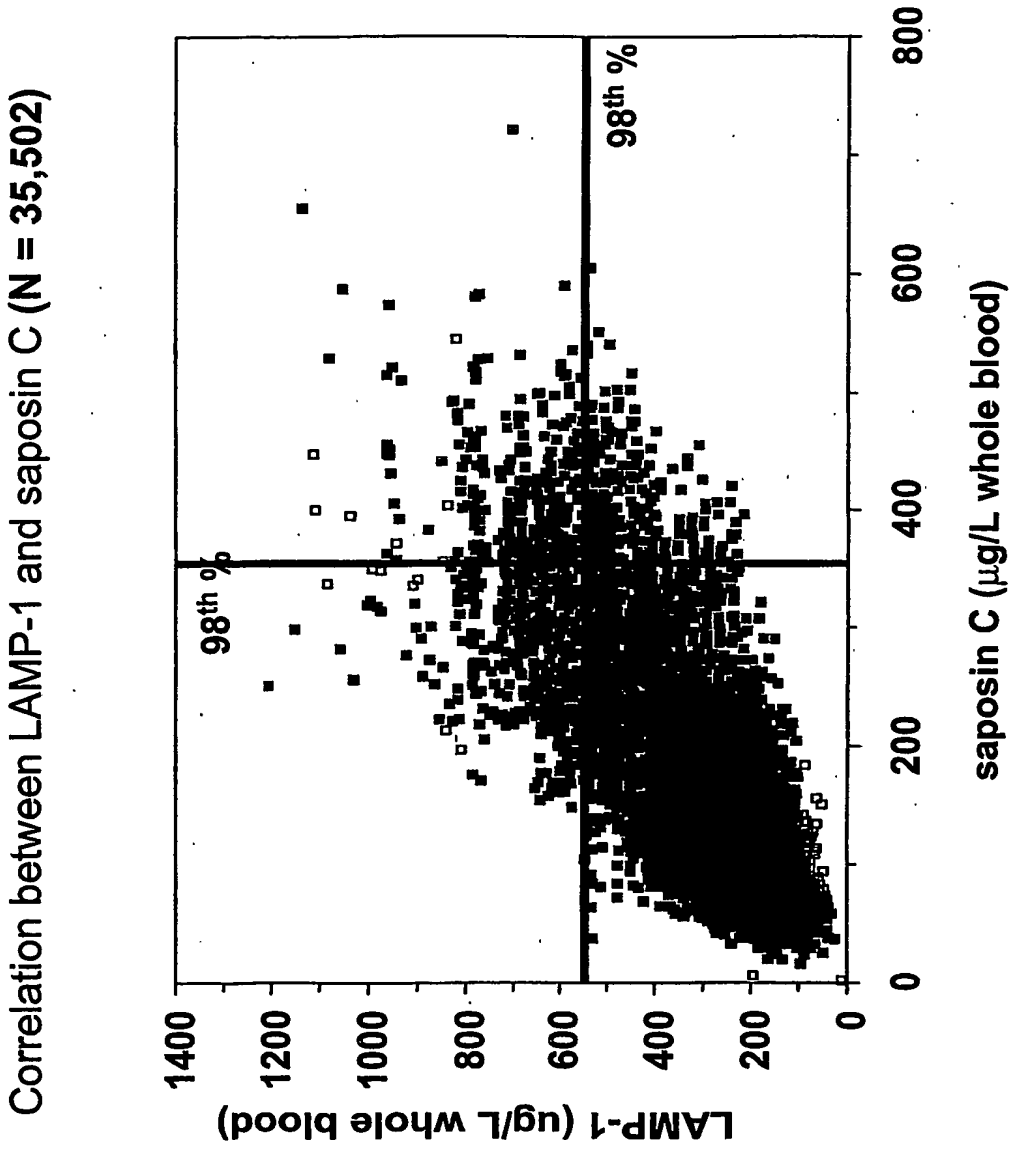
Correlation between LAMP-1 and saposin C (N = 35,502)
LAMP-1 (ug/L whole blood)
saposin C (µg/L whole blood)
98th %
98th %
0
200
400
600
800
1000
1200
1400
0
200
400
600
800

Figure 9

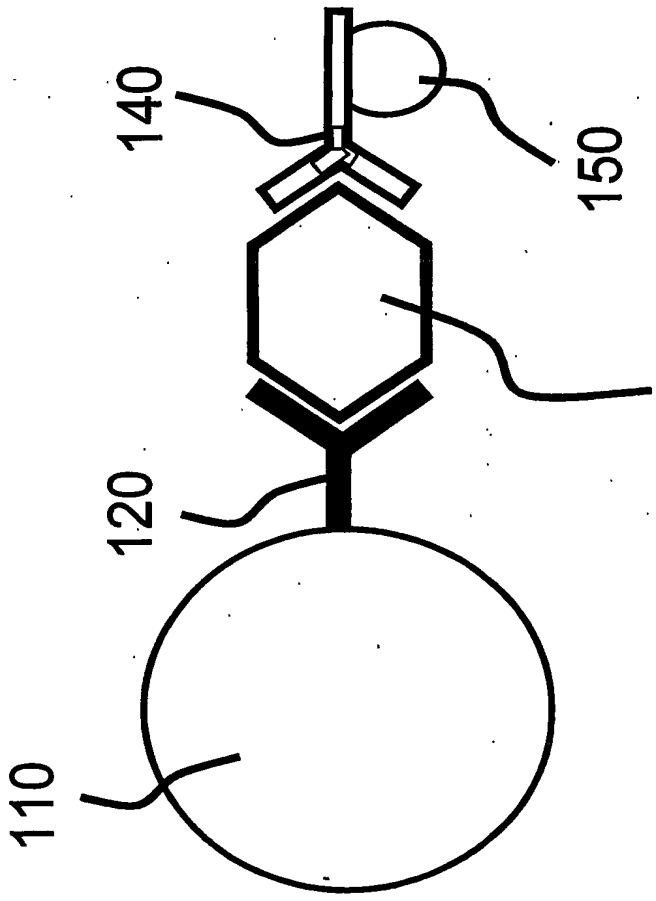

Figure 10

Antibody reagents available for lysosomal proteins

Priority	Disorder	Enzyme /Protein Marker	Protein	Polyclonal	Monoclonal (Complementary)
1		LAMP-1	CHO ex	Sheep	2
2		Saposin C		Rabbit	2
3		CD 45	commercial		
4	MPS I	α-L-iduronidase	CHO ex	Sheep	1
5	Pompe disease	α-glucosidase	CHO ex	Sheep	1
6	Gaucher disease	β-glucosidase	commercial	Sheep	1
7	Fabry disease	α-galactosidase A	commercial	Sheep	2
8	MPS VI	N-acetylgalactosamine 4-sulphatase	CHO ex	Sheep	1
9	Niemann-Pick A/B	acid sphingomyelinase	commercial	Sheep	2
10	MPS II	iduronate-2-sulphatase	CHO ex	Sheep	
11	MPS IVA	galactose 6-sulphatase	CHO ex	Rabbit	
12	MLD	arylsulphatase A	CHO ex	Sheep	
13	Krabbe disease	galactocerebrosidase			
14	MPS IIIA	heparan-N-sulphatase	CHO ex	Rabbit	1
15	MPS IIIB	α-N-acetylglucosaminidase	CHO ex	Rabbit	

Figure 11

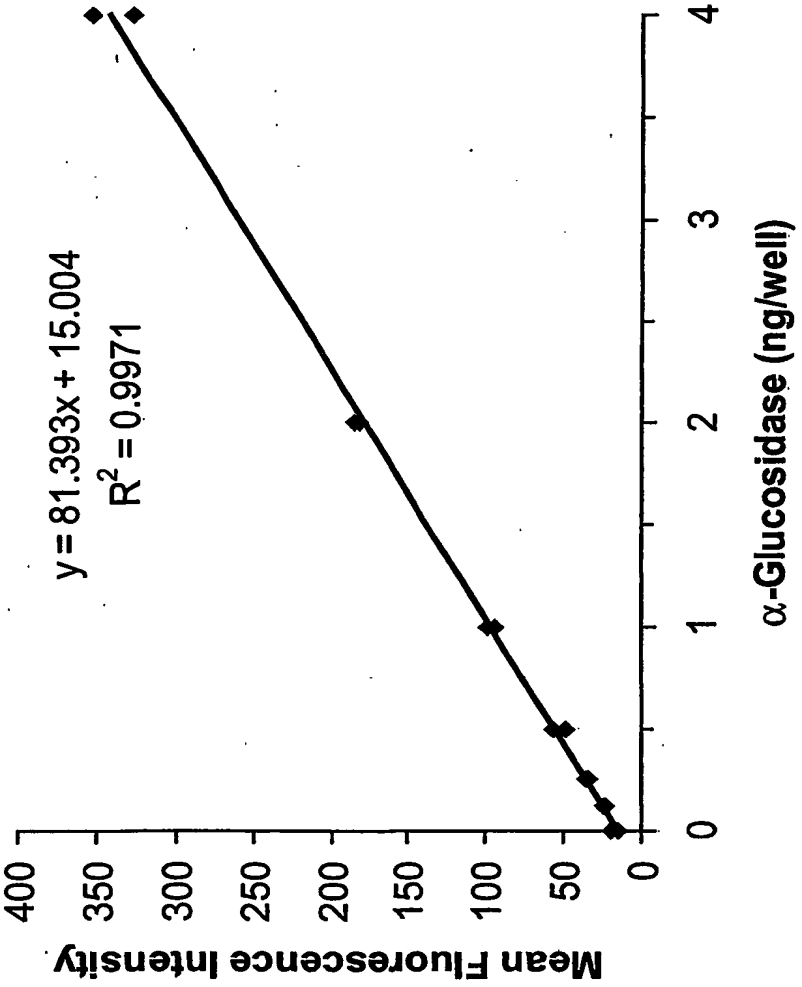
y = 81.393x + 15.004
R2 = 0.9971
Mean Fluorescence Intensity
400
350
300
250
200
150
100
50
0
0
1
2
3
4
α-Glucosidase (ng/well)

Figure 12

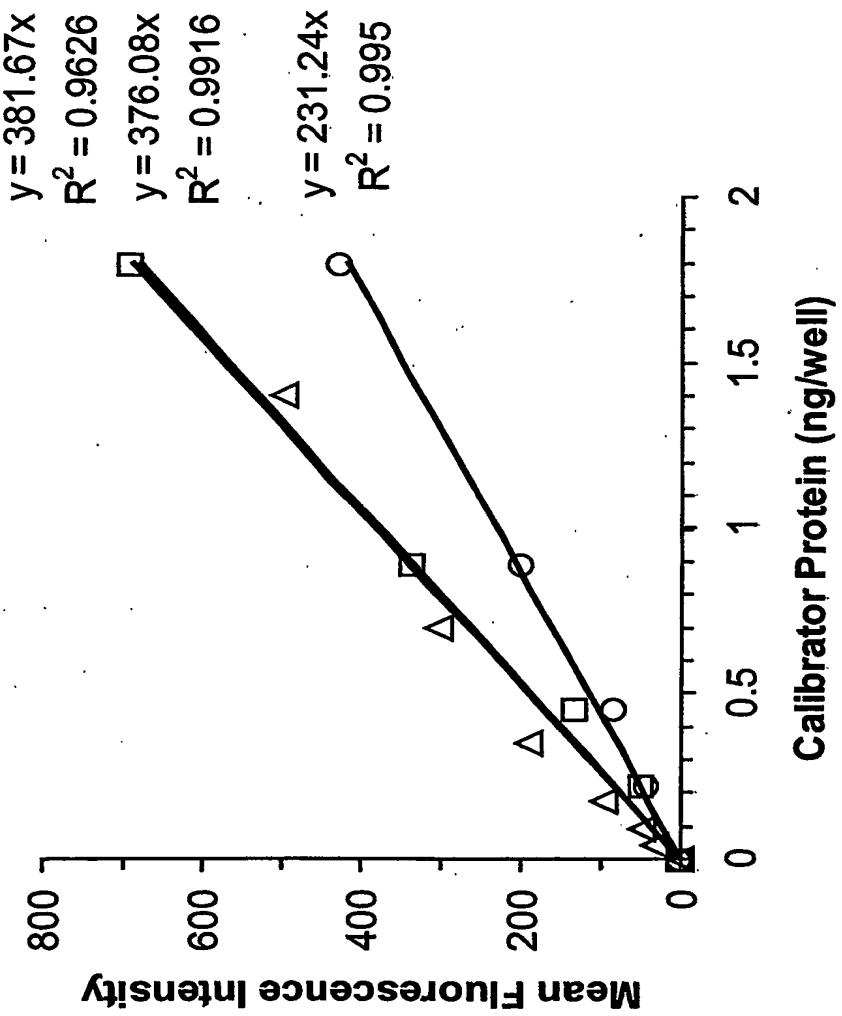
y = 381.67x
R2 = 0.9626
y = 376.08x
R2 = 0.9916
y = 231.24x
R2 = 0.995
Mean Fluorescence Intensity
800
600
400
200
0
0
0.5
1
1.5
2
Calibrator Protein (ng/well)

Figure 13

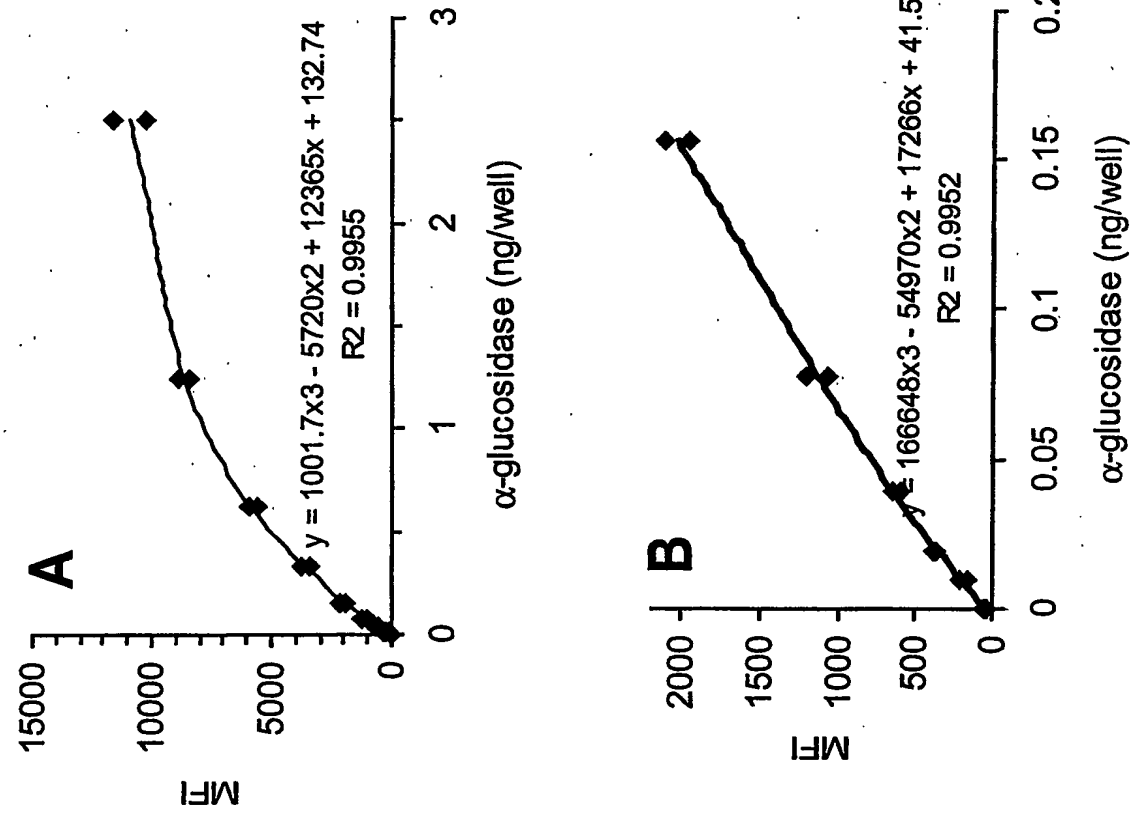
A
MFI
15000
10000
5000
0
y = 1001.7x3 - 5720x2 + 12365x + 132.74
R2 = 0.9955
0
1
2
3
α-glucosidase (ng/well)
B
MFI
2000
1500
1000
500
0
y = 166648x3 - 54970x2 + 17266x + 41.52
R2 = 0.9952
0
0.05
0.1
0.15
0.2
α-glucosidase (ng/well)

Figure 14

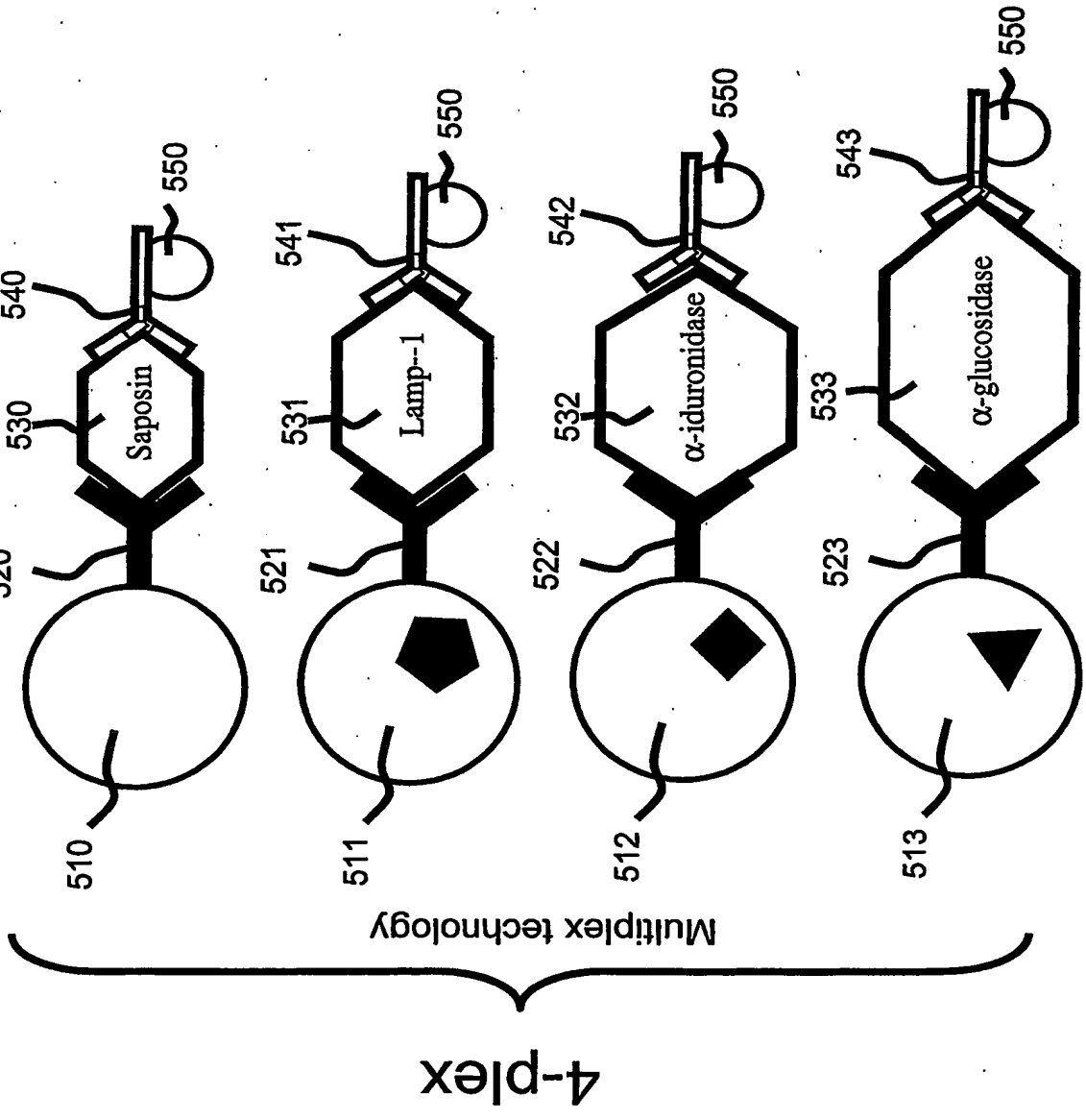
4-plex
Multiplex technology
510
511
512
513
520
521
522
523
530
531
532
533
540
541
542
543
550
550
550
550
Saposin
Lamp--1
α-iduronidase
α-glucosidase

Figure 15

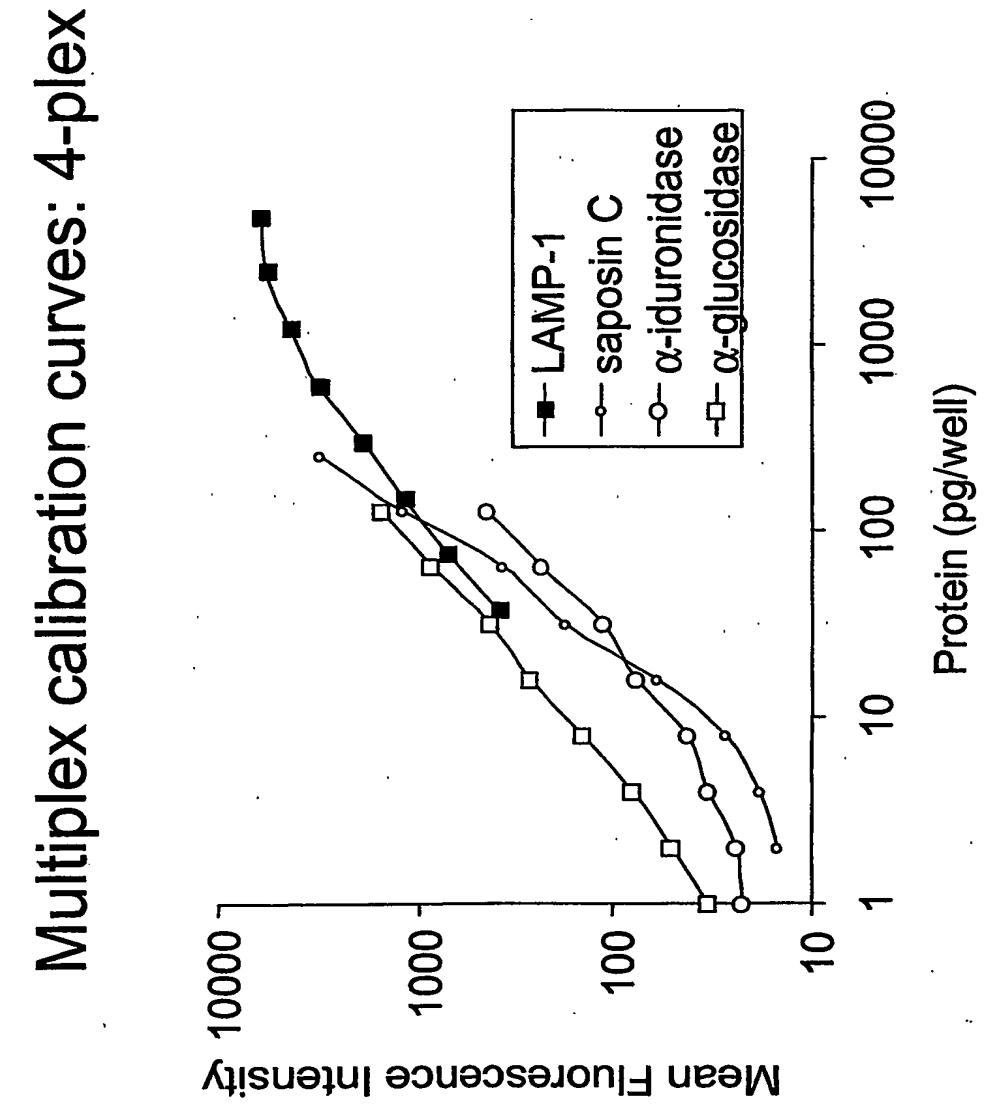
Multiplex calibration curves: 4-plex
Mean Fluorescence Intensity
10000
1000
100
10
1
10
100
1000
10000
Protein (pg/well)
LAMP-1
saposin C
α-iduronidase
α-glucosidase

Figure 16

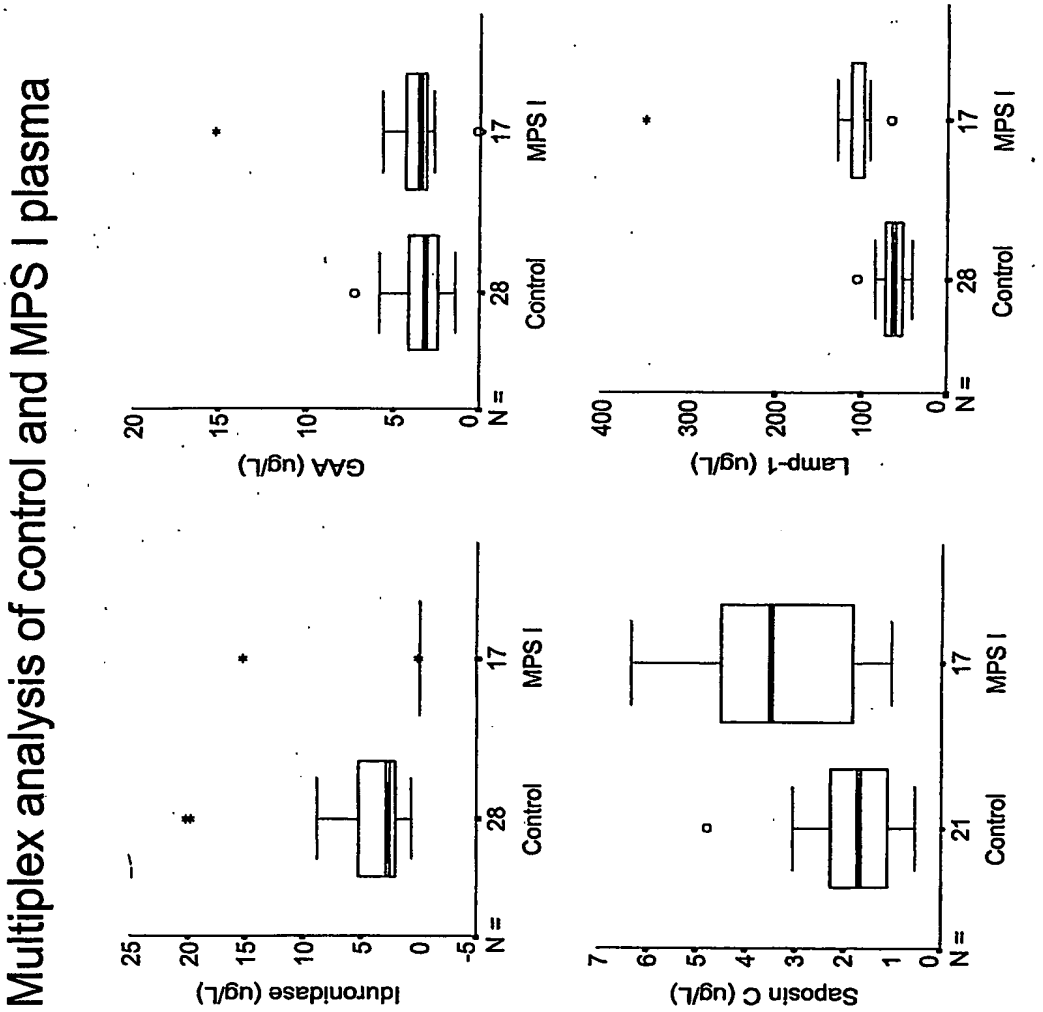
Multiplex analysis of control and MPS I plasma
GAA (ug/L)
Lamp-1 (ug/L)
Iduronidase (ug/L)
Saposin C (ug/L)
N =
28
17
21
Control
MPS I

Figure 17

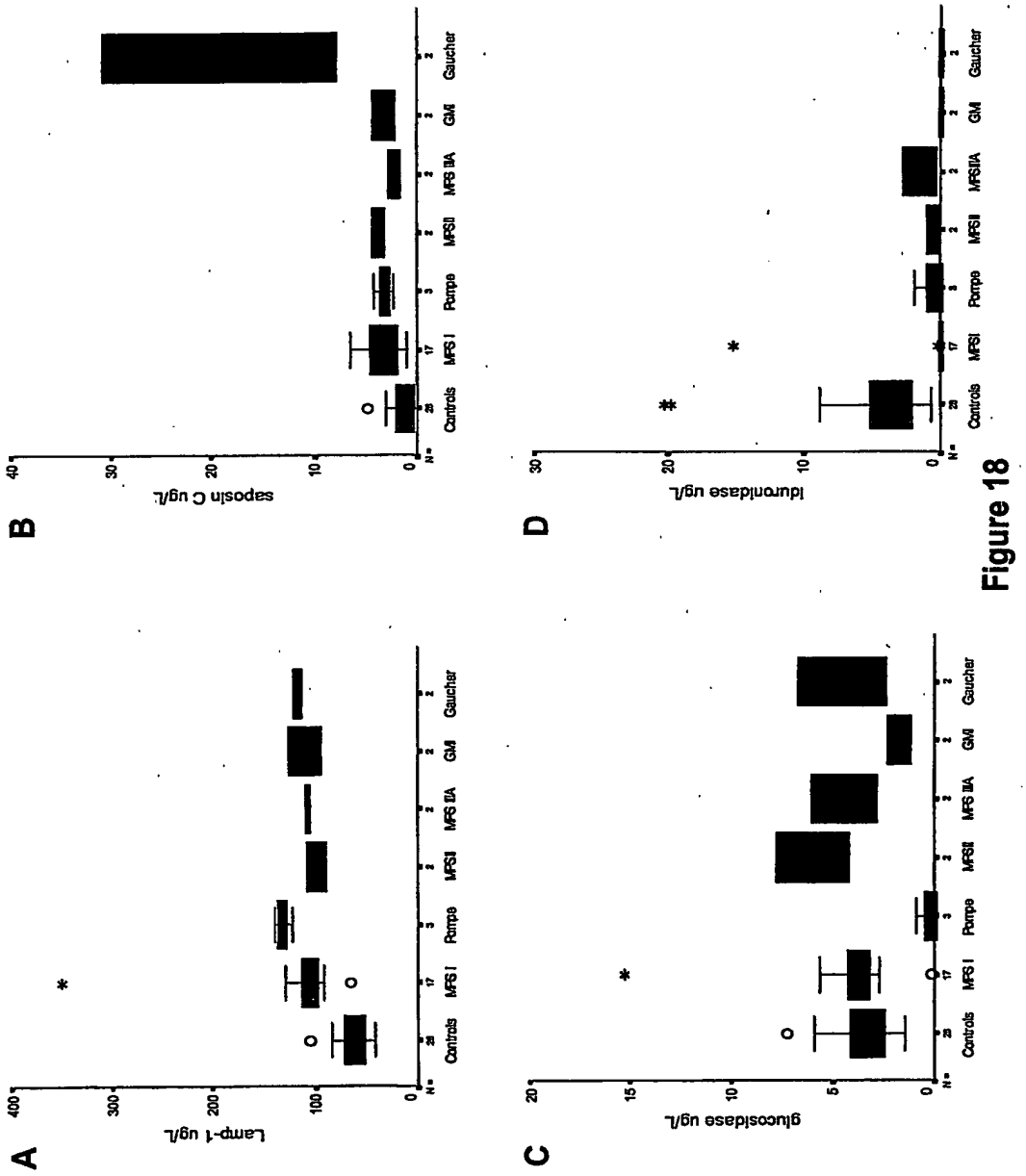
A
Lamp-1 ug/L
B
saposin C ug/L
C
glucosidase ug/L
D
Iduronidase ug/L
Controls
MPS I
Pompe
MPSII
MPS IIIA
GM
Gaucher

Figure 18

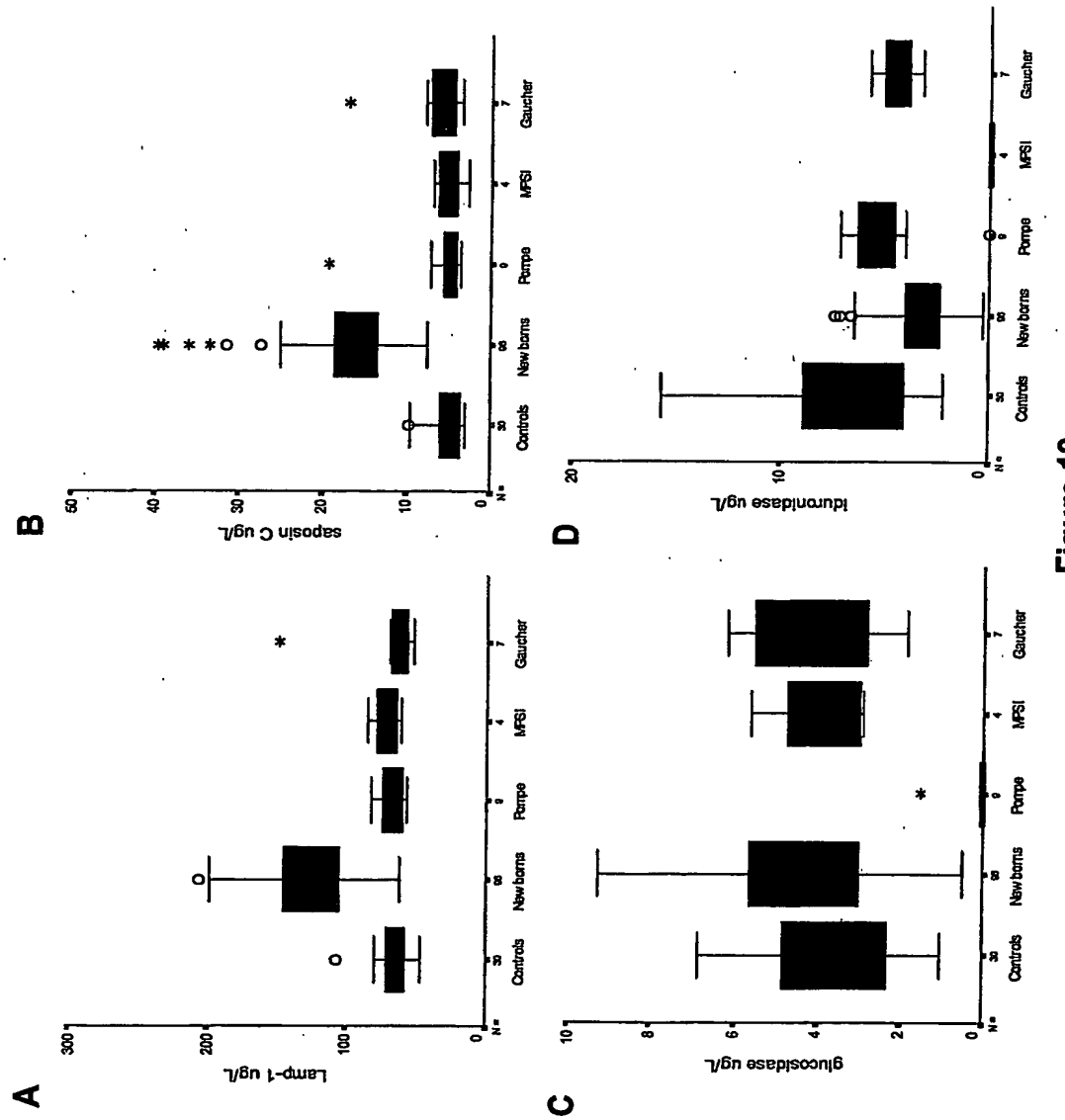
A
Lamp-1 ug/L
B
saposin C ug/L
C
glucosidase ug/L
D
Iduronidase ug/L
Controls
New borns
Pompe
MPSI
Gaucher

Figure 19

Protein markers for 7-Plex LSD screening

LAMP-1 and saposin C

Disorder	Enzyme Deficiency	Australian Prevalence	Therapy
Gaucher disease	β-glucosidase	1 in 57,000	ERT / BMT
Fabry disease	α-galactosidase A	1 in 117,000	ERT
MPS I	α-L-iduronidase	1 in 88,000	ERT / BMT
Pompe disease	α-glucosidase	1 in 146,000	ERT (trials)
MPS VI	N-acetylgalactosamine 4-sulphatase	1 in 235,000	BMT / ERT (trials)

- Most LSD patients have reduced protein.
- Total prevalence detected with 7-plex is 1 in 20,600.

Figure 20

Antibody reagents used in 7-plex assays

Assay	Bead region	Capture antibody	µg/1.25e6 beads	Reporter antibody	ng/well
Lamp-1	25	Sheep anti Lamp-1 polyclonal	9	Sheep anti Lamp-1 polyclonal	16
Saposin C	42	Monoclonal 7B2	9	Monoclonal S13C1 G2 G3	8
α-glucosidase	26	Sheep anti α-glucosidase polyclonal	5	Monoclonal 43D1	16
α-iduronidase	24	Sheep anti α-iduronidase polyclonal	36	Monoclonal Id1A	16
α-galactosidase	43	Monoclonal AG2.GG9.6.1.6	9	Monoclonal AG2.6F5.1151	32
β-glucosidase	45	Sheep anti β-glucosidase polyclonal	9	Sheep anti β-glucosidase polyclonal	32
N-acetyl-galactosamine-4-sulphatase	46	Sheep anti 4-sulphatase polyclonal	9	Sheep anti 4-sulphatase polyclonal	32

Figure 21

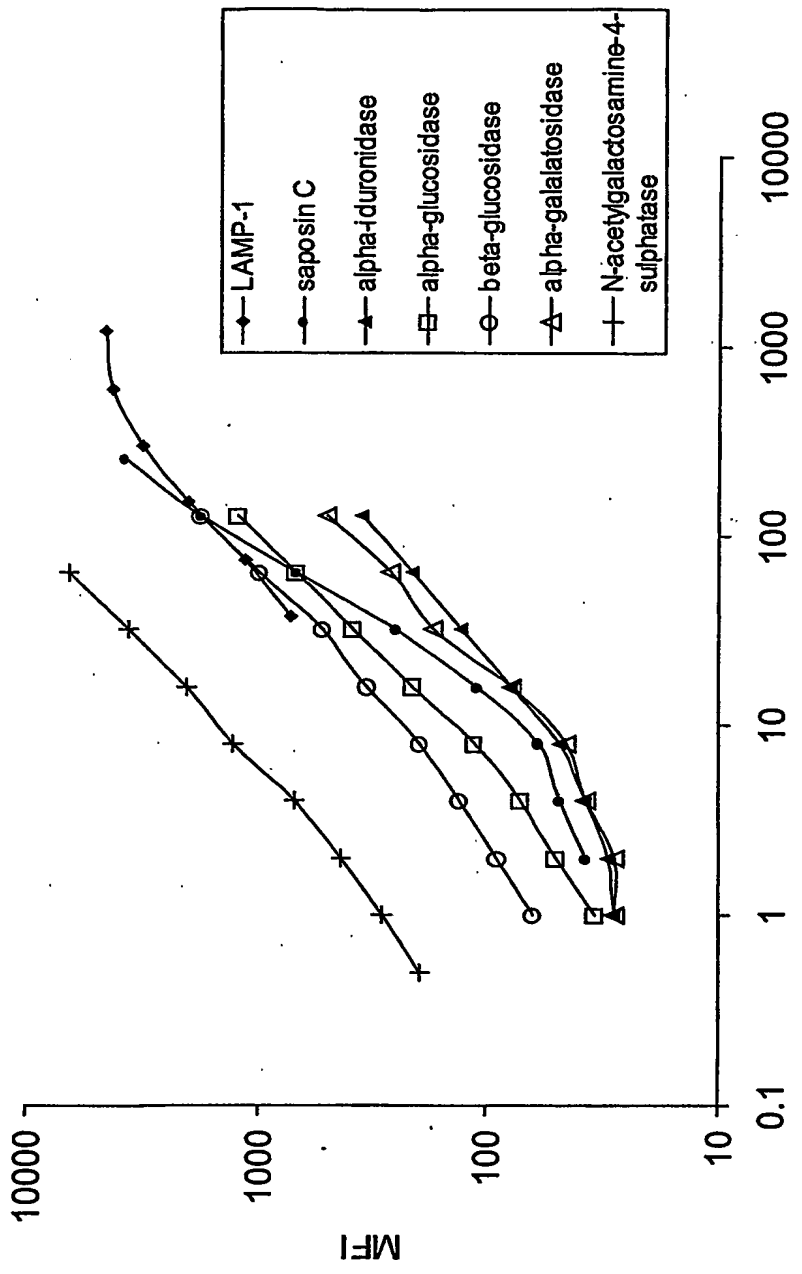
LAMP-1
saposin C
alpha-iduronidase
alpha-glucosidase
beta-glucosidase
alpha-galalatosidase
N-acetylgalactosamine-4-sulphatase
MFI
10000
1000
100
10
0.1
1
10
100
1000
10000
Protein (pg/well)

Figure 22

Adult control protein values in 7-plex assays

	Age	LAMP-1	Saposin C	α-iduronidase	α-glucosidase	β-glucosidase	α-galacto sidase	N-acetyl galactosamine-4-sulphatase
Sample ID	**years**	**ng/mL**	**ng/mL**	**ng/mL**	**ng/mL**	**ng/mL**	**ng/mL**	**ng/mL**
LDRU C7 EDTA	39.1	32.9	12.7	5.0	7.7	3.3	4.6	0.9
LDRU C9 EDTA	44.1	36.4	10.7	4.8	4.0	3.0	4.2	1.5
LDRU C11 EDTA	43.2	34.5	8.9	7.5	8.2	3.5	4.6	1.2
LDRU C12 EDTA	47.2	28.7	13.2	10.0	8.8	4.1	7.4	1.7
LDRU C13 EDTA	25.2	36.5	14.0	6.3	9.2	3.0	5.9	0.9
LDRU C14 EDTA	22.8	38.5	22.3	7.9	14.0	6.4	8.5	2.3
LDRU C15 EDTA	32.3	38.8	13.5	11.2	10.8	5.3	4.6	1.5
LDRU C16 EDTA	23.9	31.0	12.0	4.9	9.4	3.5	2.7	1.3
LDRU C17 EDTA	24.8	34.7	13.0	8.2	5.6	4.4	4.2	1.1
LDRU C18 EDTA	26.3	29.1	12.1	4.3	5.3	4.0	5.1	1.1
LDRU C19 EDTA	39.8	36.2	13.0	5.9	6.9	3.7	3.6	1.7
LDRU C20 EDTA	31.8	40.9	17.6	8.5	10.1	5.5	7.2	1.8
Average	33.4	34.9	13.6	7.0	8.3	4.1	5.2	1.4
StDev	8.9	3.8	3.4	2.2	2.7	1.1	1.7	0.4
Min	22.8	28.7	8.9	4.3	4.0	3.0	2.7	0.9
Max	47.2	40.9	22.3	11.2	14.0	6.4	8.5	2.3
StDev (MOM)	0.3	0.1	0.3	0.3	0.3	0.3	0.3	0.3
Min (MOM)	0.7	0.8	0.7	0.6	0.5	0.7	0.5	0.6
Max (MOM)	1.4	1.2	1.6	1.6	1.7	1.5	1.6	1.6

Figure 23

Newborn control protein values

	Age	LAMP-1	Saposin C	α-iduronidase	α-glucosidase	β- glucosidase	α-gal actosidase	N-acetyl galactosamine-4 sulphatase
Sample ID	years	ng/mL	ng/mL	ng/mL	ng/mL	ng/mL	ng/mL	ng/mL
Newborn 1		23.3	4.1	1.4	1.1	1.5	1.0	0.2
Newborn 2		24.9	3.9	1.8	1.4	1.3	1.3	0.2
Newborn 3		65.1	36.7	4.0	3.7	2.7	6.5	2.2
Newborn 4		72.1	58.2	1.7	12.1	5.2	13.5	2.2
Newborn 5		54.2	56.4	2.1	12.5	4.5	9.6	2.8
Newborn 6		69.0	36.6	0.9	10.2	4.1	17.8	2.0
Newborn 7		44.7	30.3	1.8	6.6	3.7	6.4	3.5
Newborn 8		19.1	3.7	1.4	1.0	0.8	1.0	0.2
Newborn 9		42.5	19.8	3.3	3.8	3.1	5.5	1.6
Newborn 10		52.6	43.9	4.1	9.4	3.9	6.6	2.4
Newborn 11		20.9	3.9	1.8	1.1	1.1	0.9	0.2
Newborn 12		36.8	34.1	1.4	6.6	2.9	5.8	2.7
Newborn 13		56.2	64.4	2.9	13.6	5.6	15.9	3.8
Newborn 14		70.5	55.7	2.8	12.9	5.0	14.4	2.7
Newborn 15		81.1	45.6	1.6	8.3	4.1	18.5	1.9
Newborn 16		63.9	54.8	3.0	12.8	5.7	12.6	2.5
Newborn 17		83.7	72.2	2.6	13.3	6.4	29.0	3.3
Newborn 18		64.8	58.4	3.9	9.4	5.7	14.3	4.8
Newborn 19		82.4	67.8	3.4	9.6	6.6	71.0	3.3
Newborn 20		69.1	61.6	5.7	21.0	6.5	14.6	3.7
Newborn 21		47.2	24.2	3.6	9.1	3.1	8.0	1.5
Newborn 22		63.2	83.9	5.6	16.7	6.4	16.6	4.8
Newborn 23		60.2	43.3	2.9	7.1	4.6	11.1	3.0
Newborn 24		70.7	31.7	2.7	11.9	4.2	22.4	2.1
Newborn 25		62.7	35.8	3.5	10.0	3.6	10.9	2.5
Newborn 26		82.4	64.5	3.4	10.1	5.4	26.9	3.3
Newborn 27		60.7	32.1	3.2	9.6	4.1	12.7	1.9
Newborn 28		86.5	74.4	2.2	18.8	16.4	72.2	4.7
Average		58.2	42.9	2.8	9.4	4.6	16.0	2.5
StDev		19.6	22.8	1.2	5.1	2.9	17.3	1.3
Min		19.1	3.7	0.9	1.0	0.8	0.9	0.2
Max		86.5	83.9	5.7	21.0	16.4	72.2	4.8
StDev(MOM)		0.3	0.5	0.4	0.5	0.6	1.1	0.5
Min (MOM)		0.3	0.1	0.3	0.1	0.2	0.1	0.1
Max (MOM)		1.5	2.0	2.0	2.2	3.6	4.5	1.9

Figure 24

Pearson correlation coefficients for protein markers in dried blood spots from newborns.

	LAMP-1	Saposin C	α-iduronidase	α-glucosidase	β-glucosidase	α-galactosidase	N-acetylgalactosamine-4-sulphatase
LAMP-1	1.00	0.82[a]	0.31	0.73[a]	0.70[a]	0.69[a]	0.68[a]
Saposin C	0.82[a]	1.00	0.47	0.85[a]	0.75[a]	0.61[a]	0.88[a]
α-iduronidase	0.31	0.47[b]	1.00	0.48[a]	0.22	0.09	0.51[a]
α-glucosidase	0.73[a]	0.85[a]	0.48[a]	1.00	0.77[a]	0.51[a]	0.77[a]
β-glucosidase	0.70[a]	0.75[a]	0.22	0.77[a]	1.00	0.81[a]	0.74[a]
α-galactosidase	0.69[a]	0.61[a]	0.09	0.51[a]	0.81[a]	1.00	0.52[a]
N-acetylgalactosamine-4-sulphatase	0.68[a]	0.88[a]	0.51[a]	0.77[a]	0.74[a]	0.52[a]	1.00

[a] $p<0.01$
[b] $p<0.05$

Figure 25

	Age	LAMP-1	Saposin C	α-iduronidase	α-glucosidase	β-glucosidase	α-galactosidase	N-acetyl galactosamine-4-sulphatase
Adult Control[a]		**ng/mL**	**ng/mL**	**ng/mL**	**ng/mL**	**ng/mL**	**ng/mL**	**ng/mL**
Average	33.4	34.9	13.6	7.0	8.3	4.1	5.2	1.4
StDev	8.9	3.8	3.4	2.2	2.7	1.1	1.7	0.4
Min	22.8	28.7	8.9	4.3	4.0	3.0	2.7	0.9
Max	47.2	40.9	22.3	11.2	14.0	6.4	8.5	2.3
Patient[b]								
Fabry	38.15	35.55	29.24[c]	2.85[d]	6.32	4.19	0.00[d]	1.95
Fabry	34.86	37.48	27.34[c]	7.76	9.94	4.30	0.00[d]	1.32
Fabry	26.95	29.56	8.60[d]	4.03[d]	5.92	2.76[d]	0.00[d]	0.57[d]
MPS I	NA	30.01	7.71[d]	0.27[d]	4.96	1.21[d]	1.87[d]	0.53[d]
MPS I	0.77	35.74	11.11	0.00[d]	6.51	2.36[d]	5.97	1.14
MPS II	3.89	52.15[c]	37.13[c]	8.90	8.21	4.04	6.99	2.28[c]
MPS VI	4.84	40.74	11.76	6.41	7.24	3.45	3.98	0.00[d]
MPS VI	NA	29.03	11.66	5.35	4.25	1.58[d]	3.43	0.00[d]
ML II/II	0.94	44.07[c]	31.60[c]	59.02[c]	27.76[c]	4.99	3.48	5.10[c]
ML II/II	1.92	44.69[c]	74.10[c]	33.66[c]	36.38[c]	8.71[c]	6.74	9.91[c]
Pompe		44.83[c]	16.56	8.49	0.13[d]	5.55	8.48	1.98
Pompe	39.21	35.89	12.73	6.54	0.19[d]	2.80[d]	3.68	2.10
Pompe	24.40	36.61	16.99	3.77[d]	0.15[d]	2.43[d]	3.78	1.47
Pompe	57.80	35.30	20.62	5.42	0.00[d]	3.89	4.03	1.41
Pompe	10.65	34.75	10.91	2.44[d]	0.00[d]	2.65[d]	12.51[c]	1.28
Pompe	8.35	34.51	15.93	4.43	0.07[d]	3.95	2.12[d]	1.06
Pompe	10.56	44.09[c]	27.31[c]	7.21	0.09[d]	4.46	8.74[c]	1.67

[a] Adult controls (n=12); [b] MPS = mucopolysaccharidosis; ML = mucolipidosis.
[c] indicates above control range; [d] indicates below control range

Figure 26

	Age	LAMP-1	Saposin C	α-iduronidase	α-glucosidas	β-glucosidase	α-galactosidase	N-acetyl galactosamine-4-sulphatase
Newborn Controls[a]		ng/mL	ng/mL	ng/mL	ng/mL	ng/mL	ng/mL	ng/mL
Average		58.2	42.9	2.8	9.4	4.6	16.0	2.5
StDev		19.6	22.8	1.2	5.1	2.9	17.3	1.3
Min		19.1	3.7	0.9	1.0	0.8	0.9	0.2
Max		86.5	83.9	5.7	21.0	16.4	72.2	4.8
Patient[b]								
Fabry	38.15	35.55	29.24	2.85	6.32	4.19	0.00[d]	1.95
Fabry	34.86	37.48	27.34	7.76[c]	9.94	4.30	0.00[d]	1.32
Fabry	26.95	29.56	8.60	4.03	5.92	2.76	0.00[d]	0.57
MPS I	NA	30.01	7.71	0.27[d]	4.96	1.21	1.87	0.53
MPS I	0.77	35.74	11.11	0.00[d]	6.51	2.36	5.97	1.14
MPS VI	4.84	40.74	11.76	6.41[c]	7.24	3.45	3.98	0.00[d]
MPS VI	NA	29.03	11.66	5.35	4.25	1.58	3.43	0.00[d]
ML II/III	0.94	44.07	31.60	59.02[c]	27.76[c]	4.99	3.48	5.10[c]
ML II/III	1.92	44.69	74.10	33.66[c]	36.38[c]	8.71	6.74	9.91[c]
Pompe		44.83	16.56	8.49[c]	0.13[d]	5.55	8.48	1.98
Pompe	39.21	35.89	12.73	6.54[c]	0.19[d]	2.80	3.68	2.10
Pompe	24.40	36.61	16.99	3.77	0.15[d]	2.43	3.78	1.47
Pompe	57.80	35.30	20.62	5.42	0.00[d]	3.89	4.03	1.41
Pompe	10.65	34.75	10.91	2.44	0.00[d]	2.65	12.51	1.28
Pompe	8.35	34.51	15.93	4.43	0.07[d]	3.95	2.12	1.06
Pompe	10.56	44.09	27.31	7.21[c]	0.09[d]	4.46	8.74	1.67

[a] Newborn controls (n=28); [b] MPS = mucopolysaccharidosis; ML = mucolipidosis.
[c] indicates above control range; [d] indicates below control range

Figure 27

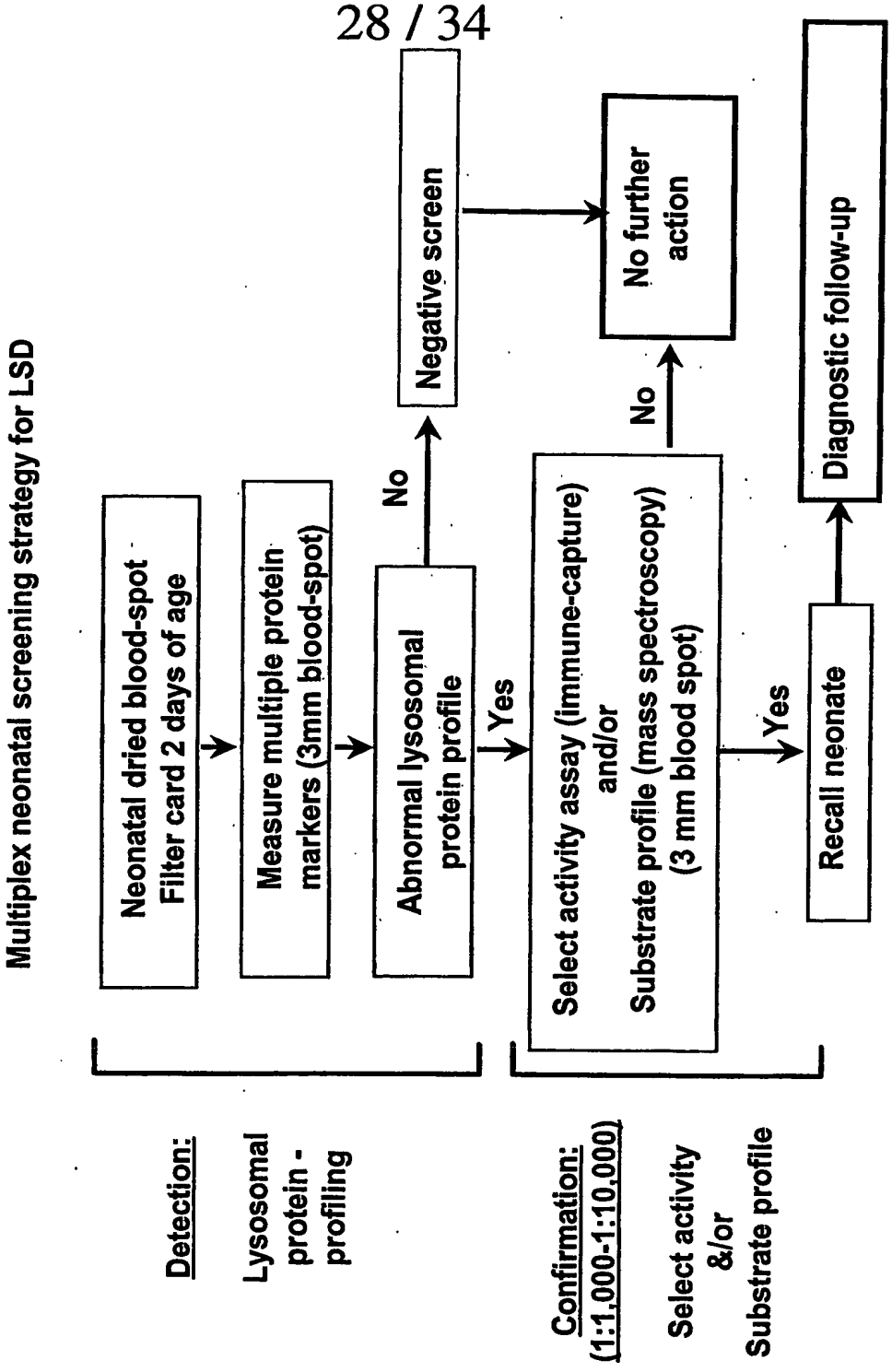
Multiplex neonatal screening strategy for LSD
Neonatal dried blood-spot
Filter card 2 days of age
Measure multiple protein markers (3mm blood-spot)
Abnormal lysosomal protein profile
No
Negative screen
No further action
Yes
Select activity assay (immune-capture) and/or
Substrate profile (mass spectroscopy)
(3 mm blood spot)
No
Yes
Recall neonate
Diagnostic follow-up
Detection:
Lysosomal protein - profiling
Confirmation:
(1:1,000-1:10,000)
Select activity &/or Substrate profile

Figure 28

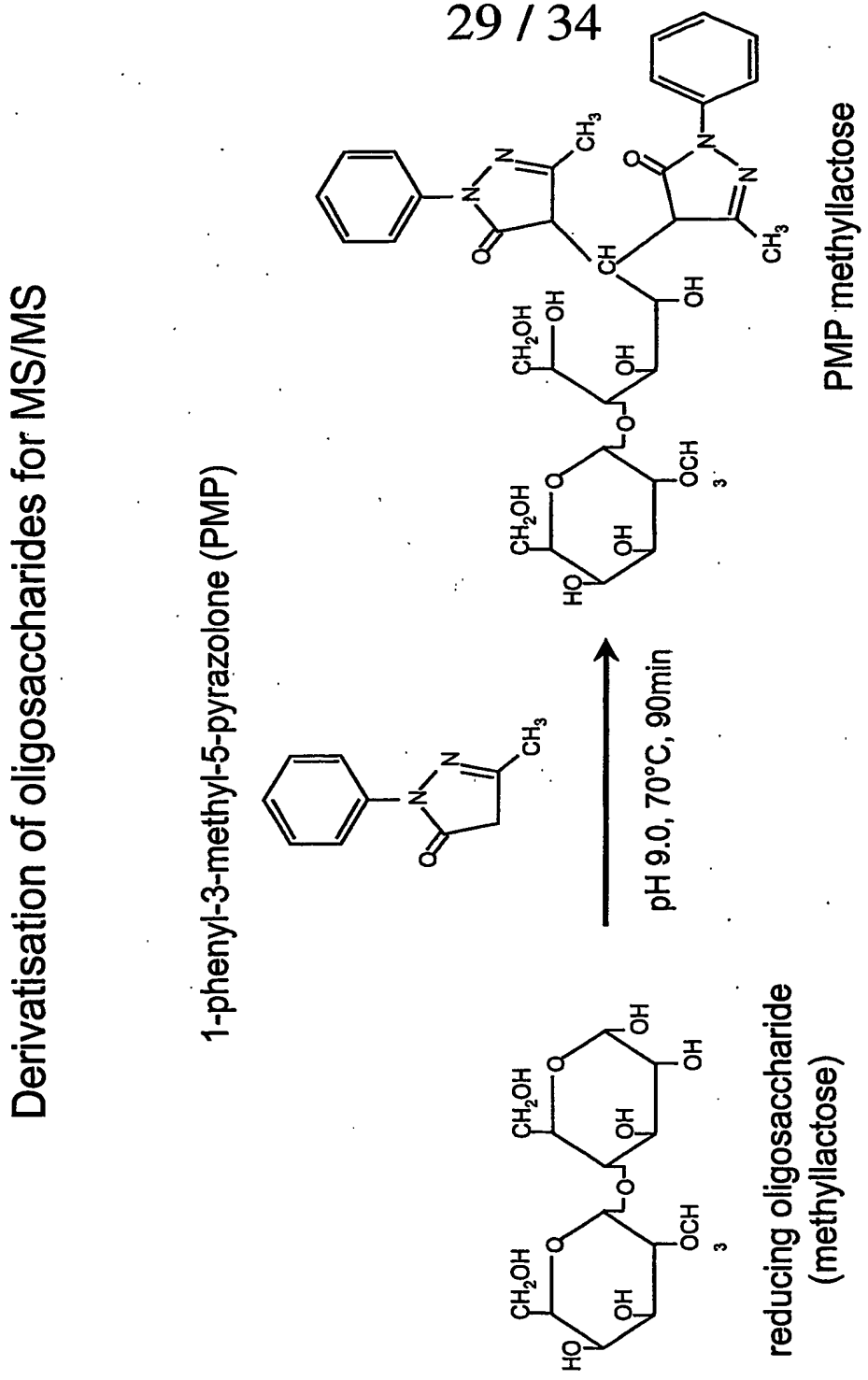
Derivatisation of oligosaccharides for MS/MS
1-phenyl-3-methyl-5-pyrazolone (PMP)
pH 9.0, 70°C, 90min
reducing oligosaccharide
(methyllactose)
PMP methyllactose

Figure 29

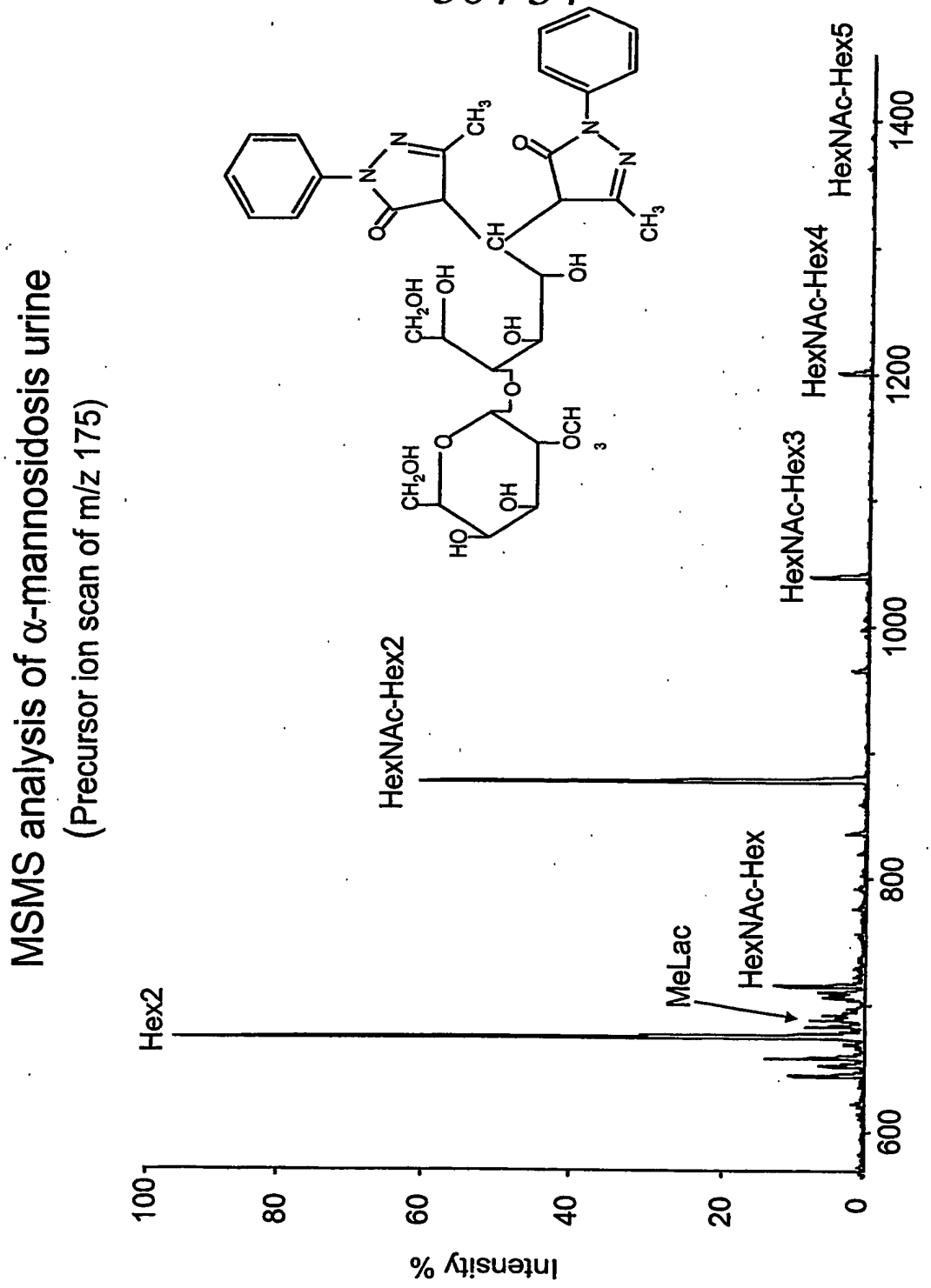
MSMS analysis of α-mannosidosis urine
(Precursor ion scan of m/z 175)
Intensity %
m/z, amu
Hex2
MeLac
HexNAc-Hex
HexNAc-Hex2
HexNAc-Hex3
HexNAc-Hex4
HexNAc-Hex5
100
80
60
40
20
0
600
800
1000
1200
1400

Figure 30

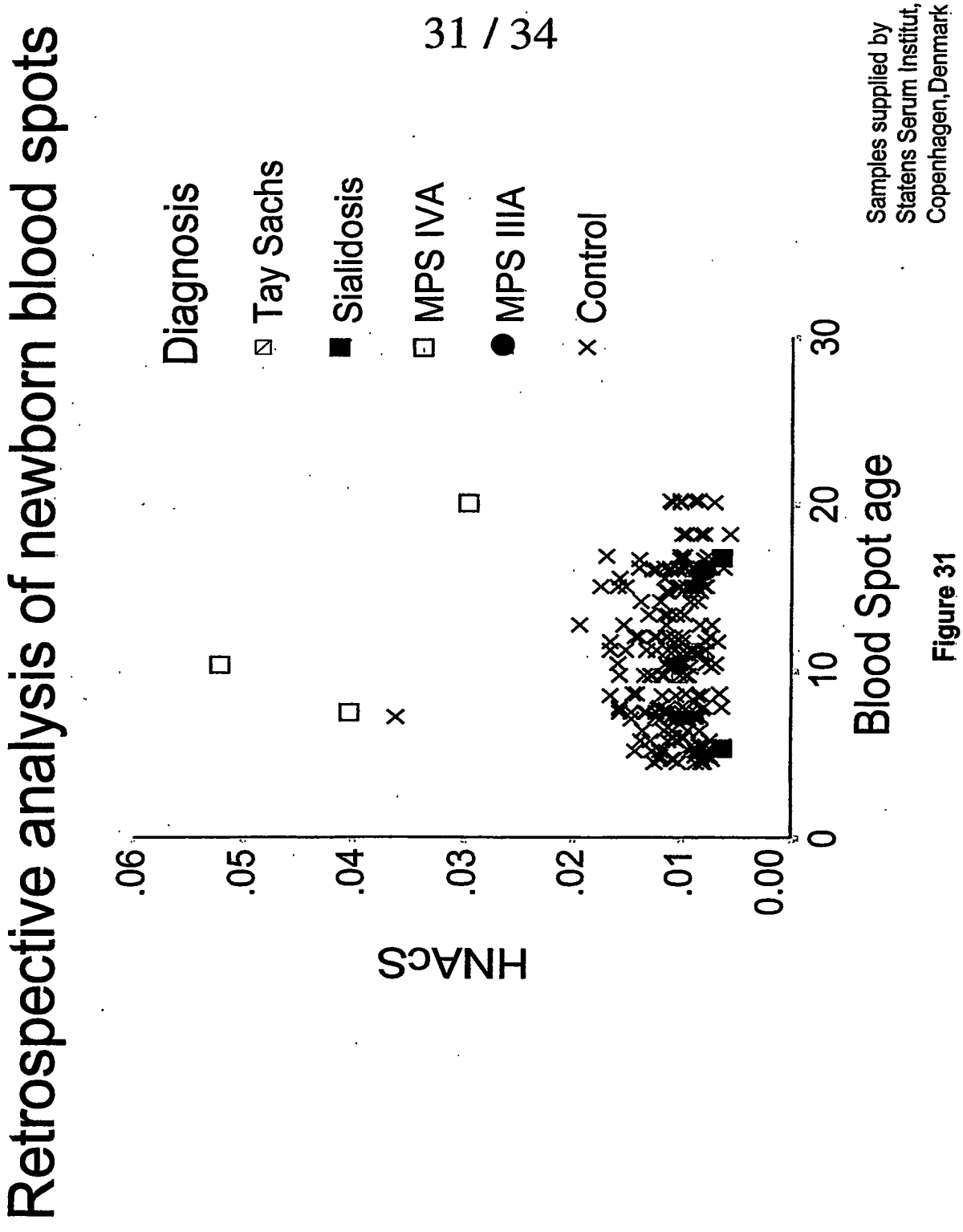
Retrospective analysis of newborn blood spots
Diagnosis
Tay Sachs
Sialidosis
MPS IVA
MPS IIIA
Control
HNAcS
.06
.05
.04
.03
.02
.01
0.00
0
10
20
30
Blood Spot age
Samples supplied by
Statens Serum Institut,
Copenhagen,Denmark

Figure 31

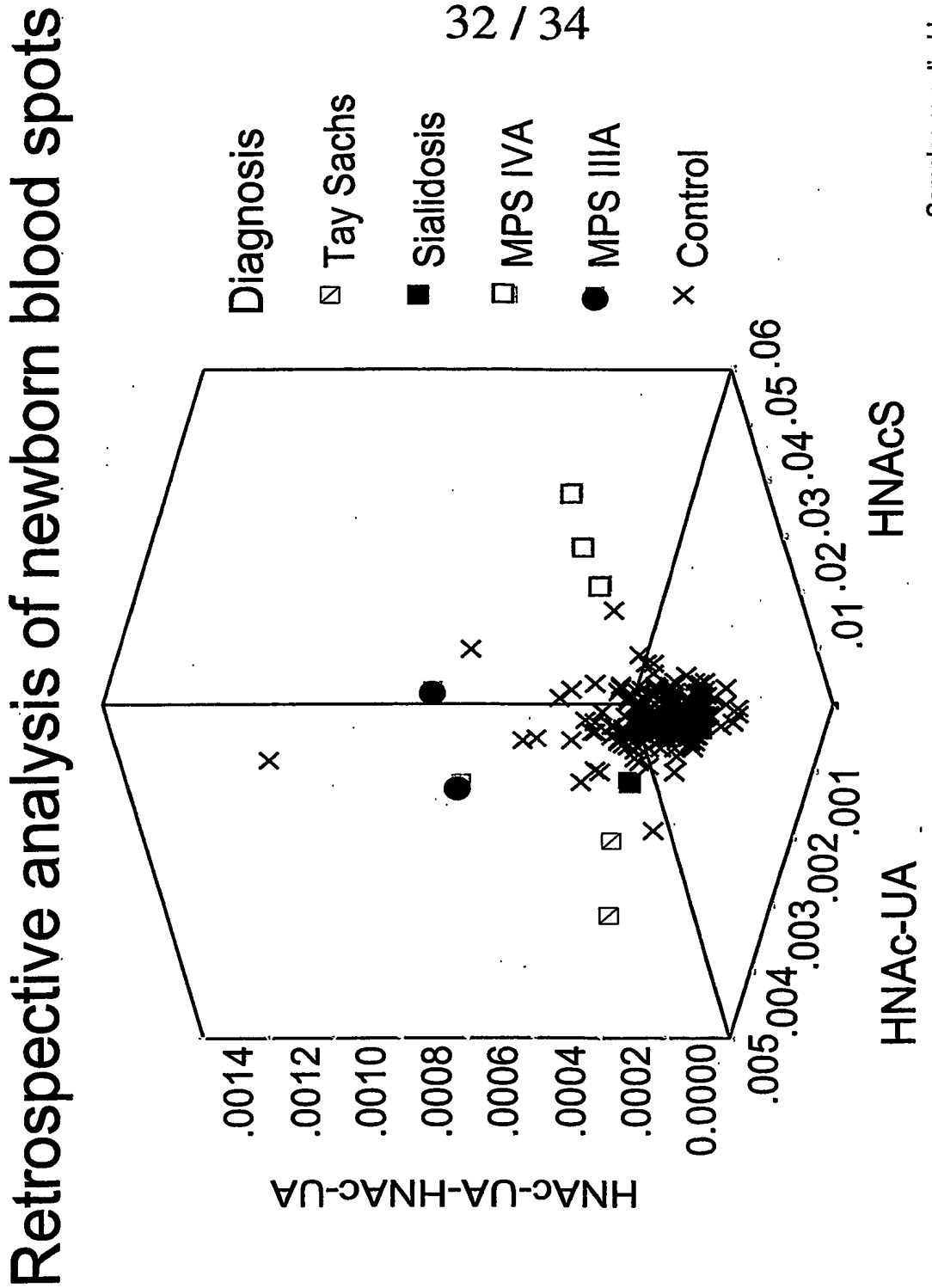
Retrospective analysis of newborn blood spots
Diagnosis
Tay Sachs
Sialidosis
MPS IVA
MPS IIIA
Control
Samples supplied by
Statens Serum Institut,
Copenhagen,Denmark
HNAc-UA-HNAc-UA
.0014
.0012
.0010
.0008
.0006
.0004
.0002
0.0000
HNAc-UA
.005
.004
.003
.002
.001
HNAcS
.01
.02
.03
.04
.05
.06

Figure 32

Summary of retrospective analysis of newborn blood spots

Disorder	n	Markers	Sensitivity/ Specificity
α-Mannosidosis	1	H2/HNAc	100 / 99.6
MPS II	4	-	-
MPS IIIA	2	HNAc-UA-HNAc-UA	100 / 100
MPS IVA	3	HNAcS	100 / 100
I-cell disease	2	GC/LC	100 / 100
Sialidosis	3	HNS-UA	67 / 100
Pompe disease	3	-	-
Sandhoff disease	6	-	-
Tay-Sachs disease	2	HNAc-UA	100 / 99.6

Figure 33

Protein markers for LSD screening

Disorder	Enzyme Deficiency	Australian Prevalence	Therapy
Gaucher disease	β-glucosidase	1 in 57,000	ERT
Fabry disease	α-galactosidase A	1 in 117,000	ERT
MPS I	α-L-iduronidase	1 in 88,000	ERT
Pompe disease	α-glucosidase	1 in 146,000	ERT (trials)
MPS VI	N-acetylgalactosamine 4-sulphatase	1 in 235,000	ERT (trials)
MPS II	iduronate-2-sulphatase	1 in 136,000	ERT (trials)
Krabbe disease	galactocerebrosidase	1 in 201,000	BMT
MLD	arylsulphatase A	1 in 92,000	BMT
MPS IVA	galactose 6-sulphatase	1 in 169,000	ERT (proposed)
Niemann-Pick type A/B	acid sphingomyelinase	1 in 248,000	ERT (proposed)
MPS IIIA	heparan-N-sulphatase	1 in 114,000	Research
MPS IIIB	α-N-acetylglucosaminidase	1 in 211,000	Research
TOTAL (n = 12)		1 in 10,500	

Figure 34